had a creatinine level of 2.30 mmol/l (26 mg/100 ml) and was presumably urine. This was confirmed by further examination in our clinical chemistry laboratory.

The cells cultured were presumably bladder epithelium. The diagnostic hazard is, of course, mistakenly concluding that the chromosome complement from such cells represents that of the fetus. Since these cells may be difficult to subculture, such an error may be more liable to occur in laboratories that examine metaphases in cell colonies from primary cultures. It is of interest that this sample was one of three of the 144 amniotic fluid specimens sent to our laboratory last year which were found to be urine. This occurred in spite of the fact that all of the amniocenteses were done with the aid of ultrasound by experienced obstetricians. It is often considered desirable for the patient's bladder to be full during this procedure, as it was in these cases, to buoy or support the uterus, especially when the placenta is anterior.² This may, of course, increase the risk of bladder puncture.

It is difficult to distinguish between urine and amniotic fluid because of the similarity in colour and appearance. An aliquot of supernatant should be tested for creatinine or urea content if the sample is suspected of being urine. Attempted cultures from all of the urine specimens we received would have been classified as culture failures if we had not been alerted by the laboratory doing our α -feto-protein determinations that the samples were not amniotic fluid.

RICHARD L NEU
J T LANMAN JUN
M WINGATE
ROBIN M BANNERMAN

Departments of Pediatrics, Medicine, and
Obstetrics and Gynecology,
State University of New York at Buffalo,
The Children's Hospital of Buffalo,
Buffalo, New York 14222

¹ Nadler, H L, and Ryan, C A, in *Human Chromosome Methodology*, ed J J Yunis, p 191. New York, Academic Press, 1974.

² Sandler, M A, Sznawajs, S M, and Bitky, L L, *Radiology*, 1979, **130**, 195.

Hulka-Clemens clips

SIR,—Had the date of the recent article by Dr G A Clarke and others (10 March, p 659) been 1 April, I would have assumed it to be some sort of hoax. However, it cannot be allowed to pass without comment.

The Hulka clips are an unreliable method of sterilisation. In this unit we have seen two patients who have become pregnant after sterilisation in this manner over the last 12 months, the operations on both patients having been completed at the hospital which has unfortunately given its name to the clip applicator. For the authors of this article to postulate abdominal transmigration of sperm on such flimsy evidence is absurd. The reality of the matter is that this is just another straightforward failure of the Hulka clip.

N TRICKEY

Heatherwood Hospital,
Ascot, Berks SL5 8AA

"Outwith my competence"

SIR,—On 3 March the word "outwith" appeared at least twice in your correspondence columns (p 616, Mr F P Jones—"outwith the scrotum"; and p 621, Professor W St C Symmers—"outwith my competence").

What does it mean? Or rather, what extra meaning does it convey that the word "out-

side" does not? The reason I address this query to you and your readers is that I have noticed the word creeping into use over the last year or so and it has always been from the mouths or pens of doctors.

The Shorter *Oxford English Dictionary* says the word is "chiefly northern, now Scots," and 50% of the examples quoted above were indeed from Aberdeen. However, before the word is exported too widely to England and becomes 1979's most fashionable new usage perhaps its usefulness could be demonstrated or its use abandoned.

KARL SABBAGH

Richmond, Surrey

*"Outwith" is widely used in educated speech in both Scotland (Mr Jones) and Northern Ireland (Professor Symmers). We feel sure that Mr Sabbagh did not insist on Scotsmen and Ulstermen who contributed to his BBC programmes using exclusively "English" English. Nor do we do so in our correspondence columns, where we try to retain the individual flavour of the contributions.—Ed, *BMJ*.

Amitriptyline plasma concentration and clinical response

SIR,—We read with interest the paper by Dr S A Montgomery and others (27 January, p 230) entitled "Amitriptyline plasma concentration and clinical response." We agree that the relationship between "plasma concentrations and clinical response is more complex" for the antidepressants than would be expected. The diverse findings of several groups with amitriptyline illustrate this point. In addition to the studies quoted, Zeigler *et al*¹ found a negative correlation between plasma concentration (total amitriptyline and nortriptyline concentration) and clinical response in 18 outpatients; Kupfer *et al*² found a negative correlation between plasma concentration (total amitriptyline and nortriptyline concentration) and clinical response in 16 inpatients; Corona *et al*³ found a positive correlation between plasma concentration and clinical effect in 77 female patients; and Vandel *et al*⁴ found a curvilinear relationship in 62 patients. We would also agree that the investigation of this relationship is a difficult problem, the sources of variation pointed out by Dr Montgomery being those most likely to give differences between groups. There is a clear need to identify responders to tricyclic antidepressant therapy and to investigate relationships between plasma values and clinical response within this group.

Several specific points from Dr Montgomery's paper need clarification. Presumably the placebo period was five to seven days, long enough to eliminate "placebo responders." The response rate was 60%, which is the usual placebo response. Were patients who responded early in the trial continued on treatment until they had completed six weeks' drug treatment? The authors made a mathematical error in that 58%, not 72%, of patients were within the 80-200 μ g/l range. What percentage of patients inside the therapeutic range actually improved and what were the criteria of improvement? Did any patients outside the "therapeutic" range improve? What proportion of individuals had plasma values less than 80 μ g/l? All would agree that not enough drug does not produce the desired clinical response, and that these patients should not be included in the regression analysis. Were any attempts

made to titrate non-responding patients' plasma values to the "therapeutic" range and measure response? The mean values of plasma amitriptyline and nortriptyline are given to two decimal places. Surely these should be quoted at best only to the nearest 5 μ g/l. We assume that these values were measured using gas chromatography by the method of Dawling and Braithwaite,⁵ which has a precision of 2.5% at "therapeutic" concentrations. Were these all new patients or had some or all been previously reported? No simple relationship between plasma concentration and age was found in this study. Nies *et al*⁶ found that steady state levels of amitriptyline were influenced by age and sex. This may be an important source of variation between studies examining relationships between plasma concentrations and clinical response. The method of measuring plasma concentrations is another source of variation. Interlaboratory comparison of assays is required.⁷

This trial highlights the problems of studies attempting to correlate plasma values and clinical response. All clinicians would agree with the general findings of the results of the study. For endogenous depressions, not enough drug does not produce a therapeutic effect; too much drug may be associated with dangerous cardiac abnormalities.⁸ This disagreement between groups is primarily concerned with defining the upper and lower limits of tricyclic antidepressant plasma concentrations.⁹ For individual patients who respond to tricyclic antidepressants a relationship between plasma concentrations and clinical response has been demonstrated.¹⁰

T R NORMAN
G D BURROWS
K P MAGUIRE

Department of Psychiatry,
University of Melbourne,
Victoria 3050

BRUCE SCOGGINS

Howard Florey Institute,
University of Melbourne,
Victoria 3050

¹ Zeigler, V, *et al*, *Clinical Pharmacology and Therapeutics*, 1976, **19**, 795.

² Kupfer, D J, *et al*, *Clinical Pharmacology and Therapeutics*, 1977, **22**, 904.

³ Corona, G L, *et al*, *Pharmacopsychiatrie*, 1977, **10**, 299.

⁴ Vandel, S, *et al*, *European Journal of Clinical Pharmacology*, 1978, **14**, 185.

⁵ Dawling, S, and Braithwaite, R A, *Journal of Chromatography*, 1978, **146**, 449.

⁶ Nies, A, *et al*, *American Journal of Psychiatry*, 1977, **134**, 790.

⁷ Burrows, G D, *et al*, *Biochemical Medicine*, 1978, **20**, 125.

⁸ Burrows, G D, *et al*, *British Journal of Psychiatry*, 1976, **129**, 335.

⁹ Burrows, G D, *et al*, *Communications in Psychopharmacology*, 1978, **2**, 393.

¹⁰ Burrows, G D, *et al*, *Clinical Pharmacology and Therapeutics*, 1974, **16**, 639.

Blood specimen collection tubes for coagulation tests

SIR,—It has been brought to our attention that unsilicified glass tubes with liquid citrate are now marketed labelled "for coagulation studies." The Anticoagulant Control Panel wishes to emphasise that use of such tubes may cause inaccurate results of coagulation tests and therefore lead to an error in diagnosis or dangerous instability in the control of anticoagulant therapy.

Blood specimens for coagulation tests should be collected with a plastic syringe and transferred to a plastic tube containing 0.109 mol/l liquid trisodium citrate, which has been freshly added in the proportion of 1